



FLWEMS Paramedic Medication Information For:

SUCCINYLCHOLINE CHLORIDE

(Anectine)

Action And Clinical Pharmacology: Succinylcholine is an ultra short-acting depolarizing-type, skeletal muscle relaxant. As does acetylcholine, it combines with the cholinergic receptors of the motor end plate to produce depolarization. This depolarization may be observed as fasciculations. Subsequent neuromuscular transmission is inhibited so long as adequate concentration of succinylcholine remains at the receptor site. Onset of flaccid paralysis is rapid, (less than 1 minute after i.v. administration), and with single administration lasts approximately 4 to 6 minutes.

Succinylcholine is rapidly hydrolyzed by plasma cholinesterase to succinylmonocholine (which possesses clinically insignificant depolarizing muscle relaxant properties) and then more slowly to succinic acid and choline (see Precautions). About 10% of the drug is excreted unchanged in the urine. The paralysis following administration of succinylcholine chloride is progressive, initially involving consecutively the levator muscles of the face, muscles of the glottis and finally the intercostals and the diaphragm and all other skeletal muscles.

Succinylcholine has no direct action on the uterus or other smooth muscle structures. Because it is highly ionized and has low fat solubility, it does not readily cross the placenta.

Tachyphylaxis occurs with repeated administration (see Precautions).

Depending on the dose and duration of succinylcholine administration, the characteristic depolarizing neuromuscular block (Phase I block) may change to a block with characteristics superficially resembling a nondepolarizing block (Phase II block). This may be associated with prolonged respiratory muscle paralysis or weakness in patients who manifest the transition to Phase II block. When this diagnosis is confirmed by peripheral nerve stimulation, it may sometimes be reversed with anticholinesterase drugs such as neostigmine (see Precautions). Anticholinesterase drugs may not always be effective. If given before succinylcholine is metabolized by cholinesterase, anticholinesterase drugs may prolong rather than shorten paralysis.

Succinylcholine has no direct effect on the myocardium. Succinylcholine stimulates both autonomic ganglia and muscarinic receptors which may cause changes in cardiac rhythm, predominantly bradycardia and occasional asystoles. Changes in rhythm including cardiac arrest, may also result from vagal stimulation, which may occur during surgical procedures, or from hyperkalemia, particularly in children (see Precautions, Children). These effects are enhanced by halogenated anesthetics.

Succinylcholine causes an increase in intraocular pressure immediately after its injection and during the fasciculation phase, and causes slight increases which may persist after onset of complete paralysis (see Warnings).

Succinylcholine may cause slight increases in intracranial pressure immediately after its injection and during the fasciculation phase (see Precautions).

As with other neuromuscular blocking agents, the potential for releasing histamine is present following succinylcholine administration. Signs and symptoms of histamine-mediated release such as flushing, hypotension and bronchoconstriction are, however, uncommon in normal clinical usage.

Succinylcholine has no effect on consciousness, pain threshold or cerebation, It should be used only with adequate anesthesia (see Warnings).

Indications And Clinical Uses: As an adjunct to general anesthesia, to facilitate tracheal intubation, and to provide skeletal muscle relaxation during surgery or mechanical ventilation.

Contra-Indications: In persons with personal or familial history of malignant hyperthermia, skeletal muscle myopathies and known hypersensitivity to the drug. It is also contraindicated in patients after the acute phase of injury following major burns, multiple trauma, extensive denervation of skeletal muscle, or upper motor neuron injury, because succinylcholine administered to such individuals may result in severe hyperkalemia which may result in cardiac arrest (see Warnings). The risk of hyperkalemia in these patients increases over time and usually peaks at 7 to 10 days after the injury. The risk is dependent on the extent

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and location of the injury. The precise time of onset and the duration of the risk period are not known. Acute rhabdomyolysis with hyperkalemia can occur when used in individuals with a skeletal muscle myopathy such as Duchenne's muscular dystrophy (see Precautions, Children). tag_WarningWarnings

Manufacturers' Warnings In Clinical States: In infants and children, especially in boys under 8 years of age, the rare possibility of inducing life-threatening hyperkalemia in undiagnosed myopathies by the use of succinylcholine must be balanced against the risk of alternative means of securing the airway.

Succinylcholine should be used only by those skilled in the management of artificial respiration and only when facilities are instantly available for tracheal intubation and for providing adequate ventilation of the patient, including the administration of oxygen under positive pressure and the elimination of carbon dioxide. The clinician must be prepared to assist or control respiration.

To avoid distress to the patient, succinylcholine should not be administered before unconsciousness has been induced. In emergency situations, however, it may be necessary to administer succinylcholine before unconsciousness is induced.

Succinylcholine is metabolized by plasma cholinesterase and should be used with caution, if at all, in patients known to be or suspected of being homozygous for the atypical plasma cholinesterase gene.

Hyperkalemia: Succinylcholine should be administered with great caution to patients suffering from hyperkalemia because in these circumstances succinylcholine may induce serious cardiac arrhythmias or cardiac arrest due to hyperkalemia.

Great caution should be observed if succinylcholine is administered to patients during the acute phase of injury following major burns, multiple trauma, extensive denervation of skeletal muscle, or upper motor neuron injury (see Contraindications). The risk of hyperkalemia in these patients increases over time and usually peaks at 7 to 10 days after the injury. The risk is dependent on the extent and location of the injury. The precise time of onset and the duration of the risk period are undetermined. Patients with chronic abdominal infection, subarachnoid hemorrhage, or conditions causing degeneration of central and peripheral nervous systems should receive succinylcholine with great caution because of the potential for developing severe hyperkalemia.

Immediate treatment of hyperkalemia should include hyperventilation, i.v. calcium, i.v. sodium bicarbonate and i.v. glucose (with or without insulin).

Malignant Hyperthermia: Succinylcholine administration has been associated with acute onset of malignant hyperthermia, a potentially fatal hypermetabolic state of skeletal muscle. The risk of developing malignant hyperthermia following succinylcholine administration increases with the concomitant administration of volatile anesthetics. Malignant hyperthermia frequently presents as intractable spasm of the jaw muscles (masseter spasm) which may progress to generalized rigidity, increased oxygen demand, tachycardia, tachypnea and profound hyperpyrexia. Successful outcome depends on recognition of early signs, such as jaw muscle spasm, increase of end-tidal carbon dioxide concentrations, or generalized rigidity to initial administration of succinylcholine for tracheal intubation, or failure of tachycardia to respond to deepening anesthesia. Skin mottling, rising temperature and coagulopathies may occur later in the course of the hypermetabolic process. In short procedures, these symptoms and signs may not appear until the patient is in the recovery room. Recognition of the syndrome is a signal for discontinuance of anesthesia, attention to increased oxygen consumption, requirement for a marked increase in minute ventilation to correct respiratory acidosis, supplementary i.v. bicarbonate to control metabolic acidosis, support of circulation, assurance of adequate urinary output and institution of measures to control rising temperature. Dantrolene sodium i.v., is recommended as an adjunct to supportive measures in the management of this problem. Consult literature references and the dantrolene prescribing information for additional information about the management of malignant hyperthermic crisis. Continuous monitoring of temperature and expired CO₂ is recommended as an aid to early recognition of malignant hyperthermia.

Other: In adults the incidence of bradycardia, which may progress to asystole, is greater after a second dose of succinylcholine. In infants and young children, bradycardia and transient asystole may occur after one

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dose of succinylcholine. The incidence and severity of bradycardia is greater in infants and children than in adults. Pretreatment with anticholinergic agents (e.g., atropine), in most cases, will reduce the occurrence of bradyarrhythmias.

Succinylcholine causes an increase in intraocular pressure. It should not be used in instances in which an increase in intraocular pressure is undesirable (e.g., narrow-angle glaucoma, penetrating eye injury) unless the potential benefit of this use outweighs the potential risk.

Succinylcholine is acidic (pH=3.5) and should not be mixed with alkaline solutions having a pH greater than 8.5 (e.g., barbiturate solutions).

Precautions: General: When succinylcholine is given over a prolonged period of time, the characteristic depolarization block of the myoneural junction (Phase I block) may change to a block with characteristics superficially resembling a non-depolarizing block (Phase II block). Prolonged respiratory muscle paralysis or weakness may be observed in patients manifesting this transition to Phase II block. The transition from Phase I to Phase II block has been reported in 7 of 7 patients studied under halothane anesthesia after an accumulated dose of 2 to 4 mg/kg succinylcholine (administered in repeated, divided doses). The onset of Phase II block coincided with the onset of tachyphylaxis and prolongation of spontaneous recovery. In another study, using balanced anesthesia (N₂O/O₂/narcotic/thiopental) and succinylcholine infusion, the transition was less abrupt, with great individual variability in the dose of succinylcholine required to produce Phase II block. Of 32 patients studied, 24 developed Phase II block. Tachyphylaxis was not associated with the transition to Phase II block, and 50% of the patients who developed Phase II block experienced prolonged recovery.

When Phase II block is suspected in cases of prolonged neuromuscular blockade, positive diagnosis should be made by peripheral nerve stimulation, prior to administration of any anticholinesterase drug. Reversal of Phase II block is a medical decision which must be made upon the basis of the individual clinical pharmacology and the experience and judgment of the physician. The presence of Phase II block is indicated by fade of responses to successive stimuli (preferably "train of four"). The use of an anticholinesterase drug to reverse Phase II block should be accompanied by appropriate doses of an anticholinergic drug to prevent disturbances of the cardiac rhythm. After adequate reversal of Phase II block with an anticholinesterase agent, the patient should be continually observed for at least 1 hour for signs of return of muscle relaxation. Reversal should not be attempted unless: (1) a peripheral nerve stimulator is used to determine the presence of Phase II block (since anticholinesterase agents will potentiate succinylcholine chloride-induced Phase I block), and (2) spontaneous recovery of muscle twitch has been observed for at least 20 minutes and has reached a plateau with further recovery proceeding slowly; this delay is to ensure complete hydrolysis of succinylcholine by cholinesterase prior to administration of the anticholinesterase agent. Should the type of block be misdiagnosed, depolarization of the type initially induced by succinylcholine, (i.e., Phase I block), will be prolonged by an anticholinesterase agent.

Succinylcholine should be employed with caution in patients with fractures or muscle spasm because the initial muscle fasciculations may cause additional trauma.

Succinylcholine may cause a transient increase in intracranial pressure; however, adequate anesthetic induction prior to administration of succinylcholine will minimize this effect.

Succinylcholine may increase intragastric pressure, which could result in regurgitation and possible aspiration of stomach contents.

Neuromuscular blockade may be prolonged in patients with hypokalemia or hypocalcemia.

Reduced Plasma Cholinesterase Activity: Succinylcholine should be used carefully in patients with reduced plasma cholinesterase (pseudocholinesterase) activity. The likelihood of prolonged neuromuscular block following administration of succinylcholine must be considered in such patients (see Dosage).

Plasma cholinesterase activity may be diminished in the presence of genetic abnormalities of plasma cholinesterase (e.g., patients heterozygous or homozygous for atypical plasma cholinesterase gene),

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pregnancy, severe liver or kidney disease, malignant tumors, infections, burns, anemia, decompensated heart disease, peptic ulcer, or myxedema. Plasma cholinesterase activity may also be diminished by chronic administration of oral contraceptives, glucocorticoids, or certain MAO inhibitors and by irreversible inhibitors of plasma cholinesterase, (e.g., organophosphate insecticides, echothiophate, and certain antineoplastic drugs).

Patients homozygous for atypical plasma cholinesterase gene (1 in 2 500 patients) are extremely sensitive to the neuromuscular blocking effect of succinylcholine. In these patients, a 5 to 10 mg test dose of succinylcholine may be administered, or neuromuscular blockage may be produced by the cautious administration of a 1 mg/mL solution of succinylcholine by i.v. drip. Apnea or prolonged muscle paralysis should be treated with controlled respiration.

Drug Interactions: Drugs which may enhance the neuromuscular blocking action of succinylcholine include: promazine, oxytocin, aprotinin, certain non-penicillin antibiotics, quinidine, b-adrenergic blockers, procainamide, lidocaine, trimethaphan, lithium carbonate, magnesium salts, quinine, chloroquine, diethylether, isoflurane, desflurane, metoclopramide and terbutaline. The presence of an inhalational anesthetic may exacerbate the side effects of succinylcholine in infants and children (see Adverse Effects).

The neuromuscular blocking effect of succinylcholine may be enhanced by drugs that reduce plasma cholinesterase activity (e.g., chronically administered oral contraceptives, glucocorticoids, or certain MAO inhibitors) or by drugs that irreversibly inhibit plasma cholinesterase (see Precautions).

If other neuromuscular blocking agents are to be used during the same procedure, the possibility of a synergistic or antagonistic effect should be considered.

Carcinogenesis, Mutagenesis, Impairment of Fertility: There have been no long-term studies performed in animals to evaluate carcinogenic potential.

Pregnancy: Teratogenic effects: Animal reproduction studies have not been conducted with succinylcholine. It is also not known whether succinylcholine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Succinylcholine should be given to a pregnant woman only if clearly needed.

Nonteratogenic Effects: Plasma cholinesterase levels are decreased by approximately 24% during pregnancy and for several days postpartum. Therefore, a higher proportion of patients may be expected to show increased sensitivity (prolonged apnea) to succinylcholine when pregnant than when nonpregnant.

Labor and Delivery: Succinylcholine is commonly used to provide muscle relaxation during delivery by cesarean section. While small amounts of succinylcholine are known to cross the placental barrier, under normal conditions the quantity of drug that enters fetal circulation after a single dose of 1 mg/kg to the mother should not endanger the fetus. However, since the amount of drug that crosses the placental barrier is dependent on the concentration gradient between the maternal and fetal circulations, residual neuromuscular blockade (apnea and flaccidity) may occur in the newborn after repeated high doses to, or in the presence of atypical plasma cholinesterase in, the mother.

Lactation: It is not known whether succinylcholine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised following succinylcholine administration to a nursing woman.

Children: There are rare reports of ventricular dysrhythmias and cardiac arrest secondary to acute rhabdomyolysis with hyperkalemia in apparently healthy infants and children who receive succinylcholine (see Warnings). Several of these individuals were subsequently found to be suffering from a myopathy such as Duchenne's muscular dystrophy whose clinical signs were not obvious. When a healthy appearing infant or child suddenly develops cardiac arrest soon after administration of succinylcholine, immediate treatment of hyperkalemia should include hyperventilation, i.v. calcium, i.v. sodium bicarbonate and i.v. glucose (with or without insulin). Treatment for acute rhabdomyolysis, including a single dose of dantrolene, should also be considered.

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Unlike in adults, the incidence of bradycardia in infants and young children is common after one dose of succinylcholine. The incidence and severity of bradycardia is greater in infants and children than in adults. Pre-treatment with anticholinergic agents, e.g., atropine, in most cases, will reduce the occurrence of bradyarrhythmias.

Adverse Reactions: Adverse reactions to succinylcholine consist primarily of an extension of its pharmacological actions. Succinylcholine causes profound muscle relaxation resulting in respiratory depression to the point of apnea; this effect may be prolonged. Hypersensitivity reactions, including anaphylaxis may occur in rare instances. The following additional adverse reactions have been reported: cardiac arrest, malignant hyperthermia, arrhythmias, bradycardia, tachycardia, hypertension, hypotension, hyperkalemia, prolonged respiratory depression or apnea, increased intraocular pressure, muscle fasciculation, jaw rigidity, postoperative muscle pain, rhabdomyolysis with possible myoglobinuric acute renal failure, excessive salivation, and rash.

Symptoms And Treatment Of Overdose: Symptoms: Overdosage with succinylcholine may result in neuromuscular block beyond the time needed for surgery and anesthesia. This may be manifested by skeletal muscle weakness, decreased respiratory reserve, low tidal volume or apnea. tag_Treatment

Treatment: The primary treatment is maintenance of a patent airway and respiratory support until recovery of normal respiration is assured. Depending on the dose and duration of succinylcholine administration, the characteristic depolarizing neuromuscular block (Phase I) may change to a block with characteristics superficially resembling a nondepolarizing block (Phase II) (see Precautions).

The decision to use neostigmine to reverse a Phase II succinylcholine-induced block depends on the judgement of the clinician in the individual case. Valuable information in regard to this decision will be gained by monitoring neuromuscular function. If neostigmine is used, its administration should be accompanied by appropriate doses of an anticholinergic agent such as atropine.

Dosage And Administration: The dosage of succinylcholine should be individualized and should always be determined by the clinician after careful assessment of the patient (see Warnings).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Solutions which are not clear and colorless should not be used.

Adults: For Short Surgical Procedures: The average dose required to produce neuromuscular blockade and to facilitate tracheal intubation is 0.6 mg/kg succinylcholine given i.v. The optimum dose will vary among individuals and may be from 0.3 to 1.1 mg/kg. Following administration of doses in this range, neuromuscular blockade develops in about 1 minute; maximum blockade may persist for about 2 minutes, after which recovery takes place within 4 to 6 minutes. However, very large doses may result in more prolonged blockade. A 5 to 10 mg test dose may be used to determine the sensitivity of the patient and the individual recovery time (see Precautions).

For Long Surgical Procedures: The dosage of succinylcholine administered by infusion depends upon the duration of the surgical procedure and the need for muscle relaxation. The average rate for an adult ranges between 2.5 and 4.3 mg/min. (The sterile powder is supplied in a Flo-Pack for i.v. solutions only.)

Solutions containing from 1 to 2 mg/mL succinylcholine have commonly been used for continuous infusion. The more dilute solution (1 mg/mL) is probably preferable from the standpoint of ease of control of the rate of administration of the drug and hence, of relaxation. This i.v. solution containing 1 mg/mL may be administered at the rate of 0.5 mg (0.5 mL) to 10 mg (10 mL)/minute to obtain the required amount of relaxation. The amount required/minute will depend upon the individual response as well as the degree of relaxation required. Avoid overburdening the circulation with a large volume of fluid. It is recommended that neuromuscular function be carefully monitored with a peripheral nerve stimulator when using succinylcholine by infusion in order to avoid overdose, detect development of Phase II block, follow its rate of recovery, and assess the effects of reversing agents (see Precautions).

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Children: The i.v. dose of succinylcholine is 2 mg/kg for infants and small children; for older children and adolescents the dose is 1 mg/kg (see Warnings and Precautions, Children).

Rarely, i.v. bolus administration of succinylcholine in infants and children may result in malignant ventricular arrhythmias and cardiac arrest secondary to acute rhabdomyolysis with hyperkalemia. In such situations, an underlying myopathy should be suspected.

I.V. bolus administration of succinylcholine in infants and young children may result in profound bradycardia or, rarely, asystole. Unlike in adults, the incidence of bradycardia in infants and children is greater after a single dose of succinylcholine. The occurrence of bradyarrhythmias, in most cases, will be reduced by pretreatment with an anticholinergic drug (e.g., atropine) (see Precautions, Children).

I.M.: If necessary, succinylcholine may be given i.m. to infants, older children or adults when a suitable vein is inaccessible. A dose of up to 3 or 4 mg/kg may be given, but not more than 150 mg total dose should be administered by this route. The onset of effect of succinylcholine given i.m. is usually observed in about 2 to 3 minutes.

Reconstituted Solutions: Flo-Pack: Succinylcholine is acidic (pH 3.5) and should not be mixed with alkaline solutions having a pH greater than 8.5 (e.g., barbiturate solutions).

Preparations containing 1 to 2 mg/mL may be prepared by adding 1 000 mg succinylcholine (the contents of 2 Anectine Sterile Powder Flo-Pack units containing 500 mg succinylcholine chloride) to 1 L or 500 mL of either of the following diluents: 5% Dextrose Injection USP; 0.9% Sodium Chloride Injection USP.

Aseptic techniques should be used to prepare the diluted product. Solutions must be used within 24 hours after preparation. Discard unused portions.

Availability And Storage: Injection: Each mL of sterile nonpyrogenic solution for i.v. use contains: succinylcholine chloride 20 mg and water for injection. The solution is made isotonic with 4.5 mg sodium chloride. The pH is adjusted to 3.5 with hydrochloric acid. Single-dose ampuls of 5 mL. Multiple-dose vials of 10 and 20 mL (also contains methylparaben 0.1% as preservative), boxes of 25. Store in refrigerator at 2 to 8°C. The multiple-dose vials are stable for up to 14 days at room temperature without significant loss of potency.

Flo-Pack: Each vial sterile powder contains: succinylcholine chloride 500 mg for preparation of i.v. solutions only. Powder does not require refrigeration. Store at 15 to 30°C.

END OF INFORMATION – NOTHING FOLLOWS